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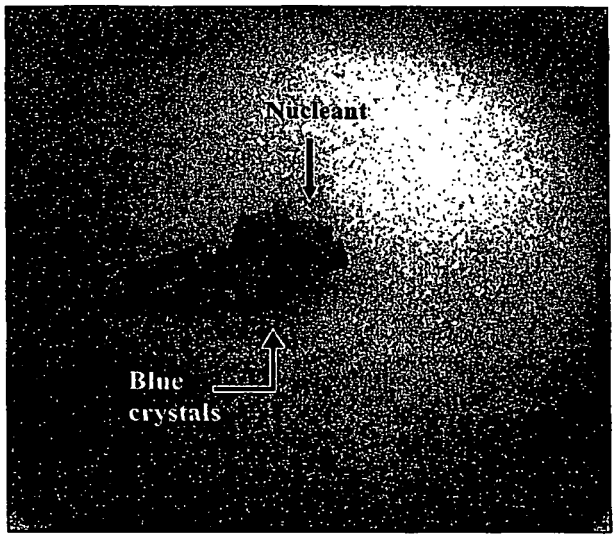
(54) Title: MESOPOROUS GLASS AS NUCLEANT FOR MACROMOLECULE CRYSTALLISATION



(57) Abstract: A method of facilitating the crystallisation of a macromolecule comprising the step of adding a mesoporous glass to a crystallisation sample wherein the mesoporous glass comprises pores having diameters between 4nm and 100nm and has a surface area of at least 50 m^2/g. A method of facilitating the crystallisation of a macromolecule comprising the step of adding to a crystallisation sample a mesoporous glass of the composition SiO_2; $CaO-P_2O_5-SiO_2$ or $Na_2O-CaO-P_2O_5-SiO_2$, wherein each of the Ca, P, Si or Na atoms within the compositions may be substituted with a suitable atom chosen from B, Al, Ti, Mg, or K, and, optionally, the composition may also include heavy elements to enhance X-ray diffraction contrast such as Ag, Au, Cr, Co, Sr, Ba, Pt, Ta or other atom with an atomic number over 20.

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Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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INTERNATIONAL SEARCH REPORT

PCT/GB 03/04875

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K1/00 G01N33/68 C30B29/58 C30B7/00 B01D9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02/088435 A (CHAYEN NAOMI ESTHER ; IMP COLLEGE INNOVATIONS LTD (GB); NEMIROVSKY YAE) 7 November 2002 (2002-11-07) see claims 1-25 and pages 18-24 the whole document	1-20, 22-24
X	CHAYEN N E ET AL: "Porous silicon: an effective nucleation-inducing material for protein crystallization" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 312, no. 4, 28 September 2001 (2001-09-28), pages 591-595, XP004451631 ISSN: 0022-2836 the whole document	1-20, 22-24

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 March 2004	06/04/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Vix, O

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHAYEN N E ET AL: "PROTEIN CRYSTALLIZATION FOR GENOMICS: TOWARDS HIGH-THROUGHPUT OPTIMIZATION TECHNIQUES" ACTA CRYSTALLOGRAPHICA SECTION D: BIOLOGICAL CRYSTALLOGRAPHY, MUNKSGAARD PUBLISHERS LTD. COPENHAGEN, DK, vol. D58, no. 6, PART 2, June 2002 (2002-06), pages 921-927, XP009013224 ISSN: 0907-4449 the whole document	1-20, 22-24
A	SAKAMOTO Y ET AL: "Direct imaging of the pores and cages of three-dimensional mesoporous materials." NATURE. 23 NOV 2000, vol. 408, no. 6811, 23 November 2000 (2000-11-23), pages 449-453, XP0002206071 ISSN: 0028-0836 cited in the application the whole document	1-20
A	SARIDAKIS E ET AL: "SEPARATING NUCLEATION AND GROWTH IN PROTEIN CRYSTALLIZATION USING DYNAMIC LIGHT SCATTERING" ACTA CRYSTALLOGRAPHICA SECTION D: BIOLOGICAL CRYSTALLOGRAPHY, MUNKSGAARD PUBLISHERS LTD. COPENHAGEN, DK, vol. 58, no. 10, PART 1, October 2002 (2002-10), pages 1597-1600, XP009013219 ISSN: 0907-4449 the whole document	1-20, 22-24
A	WIENCEK J M: "NEW STRATEGIES FOR PROTEIN CRYSTAL GROWTH" ANNUAL REVIEW OF BIOMEDICAL ENGINEERING, ANNUAL REVIEW INCO., PALO ALTO, CA, US, vol. 1, 1999, pages 505-534,1PAGE, XP009011608 the whole document	12-20, 22-24

INTERNATIONAL SEARCH REPORT

PCT/GB 03/04875

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 21 (all) and 22 (partial)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 21 (all) and 22 (partial)

Reach-through claim: 21
Present claim 21 (and part of claim 22) relate to a "crystal" defined by reference to its method of obtention.
The claim covers all possible products derived from the method claim, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for very few of such products (some of them which are known). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT).
A meaningful search cannot be established because it is not possible to determine if any of the presently known crystal of macromolecule is falling under the terms of these "crystal" product claim. Besides it is noted, that the crystals of claim 21 are not rendered novel just because of the fact that the crystals have been obtained by the method of claims 1-3 or 17-21, e.g. such crystals and their specific use can already exist.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/GB 03/04875

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02088435 A	07-11-2002	WO 02088435 A1	07-11-2002